

**CLAIMS:**

1. A pharmaceutical co-crystal composition, comprising: an API and a co-crystal former, wherein the API is a liquid or a solid at room temperature and the co-crystal former is a solid at room temperature, and wherein the API and co-crystal former are hydrogen bonded to each other.
  
2. The pharmaceutical co-crystal composition according to claim 1, wherein:
  - (a) the co-crystal former is selected from a co-crystal former of Table I or Table II;
  - (b) the API is selected from an API of Table IV;
  - (c) the API is selected from an API of Table IV and the co-crystal former is selected from a co-crystal former of Table I or Table II;
  - (d) the API is a liquid at room temperature;
  - (e) the API is a solid at room temperature;
  - (f) the API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
  - (g) the co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;

- (h) the difference in  $pK_a$  between the API and the co-crystal former does not exceed 2;
- (i) the solubility of the co-crystal is increased as compared to the API;
- (j) the dose response of the co-crystal is increased as compared to the API;
- (k) the dissolution of the co-crystal is increased as compared to the API;
- (l) the bioavailability of the co-crystal is increased as compared to the API;
- (m) the stability of the co-crystal is increased as compared to the API;
- (n) a difficult to salt or unsaltable API is incorporated into the co-crystal;
- (o) the hygroscopicity of the co-crystal is decreased as compared to the API;
- (p) an amorphous API is crystallized as a component of the co-crystal;
- (q) the form diversity of the co-crystal is decreased as compared to the API; or
- (r) the morphology of the co-crystal is modulated as compared to the API.

3. A pharmaceutical co-crystal composition, comprising: an API, a co-crystal former, and a third molecule; wherein the API is a liquid or a solid at room temperature and the co-crystal former is a solid at room temperature, and wherein the API and the third molecule are bonded to each other, and further wherein the co-crystal former and the third molecule are hydrogen bonded to each other.

4. The pharmaceutical co-crystal composition according to claim 3, wherein:

- (a) the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (b) the API is selected from an API of Table IV;
- (c) the API is selected from an API of Table IV and the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) the API is a liquid at room temperature;
- (e) the API is a solid at room temperature;
- (f) the API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone,

- thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (g) the co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine; or
  - (h) the difference in pK<sub>a</sub> between the API and the co-crystal former does not exceed 2;
  - (i) the solubility of the co-crystal is increased as compared to the API;
  - (j) the dose response of the co-crystal is increased as compared to the API;
  - (k) the dissolution of the co-crystal is increased as compared to the API;
  - (l) the bioavailability of the co-crystal is increased as compared to the API;
  - (m) the stability of the co-crystal is increased as compared to the API;
  - (n) a difficult to salt or unsaltable API is incorporated into the co-crystal;
  - (o) the hygroscopicity of the co-crystal is decreased as compared to the API;
  - (p) an amorphous API is crystallized as a component of the co-crystal;
  - (q) the form diversity of the co-crystal is decreased as compared to the API; or
  - (r) the morphology of the co-crystal is modulated as compared to the API.

5. A pharmaceutical co-crystal composition, comprising: a first and a second API, wherein each API is either a liquid or a solid at room temperature, and wherein the APIs are hydrogen bonded to a molecule.
6. The pharmaceutical co-crystal composition according to claim 5, wherein:
- (a) the first API is hydrogen bonded to the second API;
  - (b) an API is selected from an API of Table IV;
  - (c) each API is selected from an API of Table IV;
  - (d) an API is a liquid at room temperature and the other API is a solid at room temperature;
  - (e) each API is a solid at room temperature;
  - (f) an API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
  - (g) each API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
  - (h) the difference in pK<sub>a</sub> between the first API and the second API does not exceed 2;
  - (i) the solubility of the co-crystal is increased as compared to the API;
  - (j) the dose response of the co-crystal is increased as compared to the API;

- (k) the dissolution of the co-crystal is increased as compared to the API;
- (l) the bioavailability of the co-crystal is increased as compared to the API;
- (m) the stability of the co-crystal is increased as compared to the API;
- (n) a difficult to salt or unsaltable API is incorporated into the co-crystal;
- (o) the hygroscopicity of the co-crystal is decreased as compared to the API;
- (p) an amorphous API is crystallized as a component of the co-crystal;
- (q) the form diversity of the co-crystal is decreased as compared to the API; or
- (r) the morphology of the co-crystal is modulated as compared to the API.

7. A pharmaceutical co-crystal composition, comprising: a first and a second co-crystal former, wherein each co-crystal former is a solid at room temperature, and wherein both co-crystal formers are hydrogen bonded to a molecule.

8. The pharmaceutical co-crystal composition according to claim 7, wherein:

- (a) the first co-crystal former is hydrogen bonded to the second co-crystal former;
- (b) a co-crystal former is selected from a co-crystal former of Table I or Table II;
- (c) each co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) a co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;

- (e) each co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (f) the difference in pK<sub>a</sub> between the first co-crystal former and the second co-crystal former does not exceed 2;
- (g) the solubility of the co-crystal is increased as compared to the API;
- (h) the dose response of the co-crystal is increased as compared to the API;
- (i) the dissolution of the co-crystal is increased as compared to the API;
- (j) the bioavailability of the co-crystal is increased as compared to the API;
- (k) the stability of the co-crystal is increased as compared to the API;
- (l) a difficult to salt or unsaltable API is incorporated into the co-crystal;
- (m) the hygroscopicity of the co-crystal is decreased as compared to the API;
- (n) an amorphous API is crystallized as a component of the co-crystal;
- (o) the form diversity of the co-crystal is decreased as compared to the API; or
- (p) the morphology of the co-crystal is modulated as compared to the API.

9. The pharmaceutical co-crystal composition according to claim 1, wherein the API is selected from celecoxib, carbamazepine, itraconazole, olanzapine, topiramate, modafinil, 5-fluorouracil, hydrochlorothiazide, acetaminophen, aspirin, flurbiprofen, phenytoin, or ibuprofen.

10. The pharmaceutical co-crystal composition according to claim 1, further comprising a pharmaceutically acceptable diluent, excipient, or carrier.

11. A co-crystal comprising an API and a co-crystal former selected from:
- (a) carbamazepine and saccharin;
  - (b) carbamazepine and nicotinamide;
  - (c) carbamazepine and trimesic acid;
  - (d) celecoxib and nicotinamide;
  - (e) olanzapine and nicotinamide;
  - (f) celecoxib and 18-crown-6;
  - (g) itraconazole and succinic acid;
  - (h) itraconazole and fumaric acid;
  - (i) itraconazole and tartaric acid;
  - (j) itraconazole and malic acid;
  - (k) itraconazoleHCl and tartaric acid;
  - (l) modafinil and malonic acid;
  - (m) modafinil and benzamide;
  - (n) modafinil and mandelic acid;
  - (o) modafinil and glycolic acid;
  - (p) modafinil and fumaric acid;
  - (q) modafinil and maleic acid;
  - (r) topiramate and 18-crown-6;
  - (s) 5-fluorouracil and urea;
  - (t) hydrochlorothiazide and nicotinic acid;
  - (u) hydrochlorothiazide and 18-crown-6;
  - (v) hydrochlorothiazide and piperazine;
  - (w) acetaminophen and 4,4'-bipyridine;
  - (x) phenytoin and pyridone;
  - (y) aspirin and 4,4'-bipyridine;
  - (z) ibuprofen and 4,4'-bipyridine;
  - (aa) flurbiprofen and 4,4'-bipyridine;
  - (bb) flurbiprofen and trans-1,2-bis(4-pyridyl) ethylene;
  - (cc) carbamazepine and p-phthalaldehyde;
  - (dd) carbamazepine and 2,6-pyridinecarboxylic acid;
  - (ee) carbamazepine and 5-nitroisophthalic acid;
  - (ff) carbamazepine and 1,3,5,7-adamantane tetracarboxylic acid; or

(gg) carbamazepine and benzoquinone.

12. A process for preparing a pharmaceutical co-crystal composition comprising an API and a co-crystal former, comprising:

- (a) providing an API and a co-crystal former, wherein the API is a liquid or a solid at room temperature and the co-crystal former is a solid at room temperature;
- (b) grinding, heating, or contacting in solution the API with the co-crystal former under crystallization conditions, so as to form a solid phase, wherein the API and co-crystal former are hydrogen bonded to each other;
- (c) isolating co-crystals formed thereby; and
- (d) incorporating the co-crystals into a pharmaceutical composition.

13. The process of claim 12, wherein:

- (a) the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (b) the API is selected from an API of Table IV;
- (c) the API is selected from an API of Table IV and the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) the API is a liquid at room temperature;
- (e) the API is a solid at room temperature;
- (f) the API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (g) the co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester,



- ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine; or
- (h) the difference in pK<sub>a</sub> between the API and the co-crystal former does not exceed 2.

14. A process for preparing a pharmaceutical co-crystal composition comprising an API, a co-crystal former, and a third molecule, comprising:

- (a) providing an API and a co-crystal former, wherein the API is a liquid or a solid at room temperature and the co-crystal former is a solid at room temperature;
- (b) grinding, heating, or contacting in solution the API with the co-crystal former under crystallization conditions, so as to form a solid phase, wherein the API and the third molecule are bonded to each other, and further wherein the co-crystal former and the third molecule are hydrogen bonded to each other;
- (c) isolating co-crystals formed thereby; and
- (d) incorporating the co-crystals into a pharmaceutical composition.

15. The process of claim 14, wherein:

- (a) the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (b) the API is selected from an API of Table IV;
- (c) the API is selected from an API of Table IV and the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) the API is a liquid at room temperature;
- (e) the API is a solid at room temperature;
- (f) the API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic

- acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (g) the co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine; or
- (h) the difference in pK<sub>a</sub> between the API and the co-crystal former does not exceed 2.
16. A process for preparing a pharmaceutical co-crystal composition comprising a first and a second API, comprising:
- providing a first and a second API, wherein each API is either a liquid or a solid at room temperature;
  - grinding, heating, or contacting in solution the APIs under crystallization conditions, so as to form a solid phase, wherein the APIs are hydrogen bonded to a molecule;
  - isolating co-crystals formed thereby; and
  - incorporating the co-crystals into a pharmaceutical composition.
17. The process of claim 16, wherein:
- the first API is hydrogen bonded to the second API;
  - an API is selected from an API of Table IV;
  - each API is selected from an API of Table IV;
  - an API is a liquid at room temperature and the other API is a solid at room temperature;
  - each API is a solid at room temperature;

- (f) an API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (g) each API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine; or
- (h) the difference in pK<sub>a</sub> between the first API and the second API does not exceed 2.

18. A process for preparing a pharmaceutical co-crystal composition comprising a first and a second co-crystal former, comprising:

- (a) providing a first and a second co-crystal former, wherein each co-crystal former is a solid at room temperature;
- (b) grinding, heating, or contacting in solution the co-crystal formers under crystallization conditions, so as to form a solid phase, wherein both co-crystal formers are hydrogen bonded to a molecule;
- (c) isolating co-crystals formed thereby; and
- (d) incorporating the co-crystals into a pharmaceutical composition.

19. The process of claim 18, wherein:

- (a) the first co-crystal former is hydrogen bonded to the second co-crystal former;

- (b) a co-crystal former is selected from a co-crystal former of Table I or Table II;
- (c) each co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) a co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (e) each co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp<sup>2</sup> amine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine; or
- (f) the difference in pK<sub>a</sub> between the first co-crystal former and the second co-crystal former does not exceed 2.

20. The process of claim 12, wherein the API is selected from celecoxib, carbamazepine, itraconazole, olanzapine, topiramate, modafinil, 5-fluorouracil, hydrochlorothiazide, acetaminophen, aspirin, flurbiprofen, phenytoin, or ibuprofen.

21. The process of claim 12, further comprising: incorporating a pharmaceutically acceptable diluent, excipient, or carrier.

22. A process of preparing a co-crystal comprising an API and a co-crystal former, comprising:

- (a) providing an API and a co-crystal former;
- (b) grinding, heating, or contacting in solution the API with the co-crystal former under crystallization conditions, so as to form a solid phase; and
- (c) isolating co-crystals formed thereby;

wherein the API and the co-crystal former are selected from carbamazepine and saccharin, carbamazepine and nicotinamide, carbamazepine and trimesic acid, celecoxib and nicotinamide, olanzapine and nicotinamide, celecoxib and 18-crown-6, itraconazole and succinic acid, itraconazole and fumaric acid, itraconazole and tartaric acid, itraconazole and malic acid, itraconazoleHCl and tartaric acid, modafinil and malonic acid, modafinil and benzamide, modafinil and mandelic acid, modafinil and glycolic acid, modafinil and fumaric acid, modafinil and maleic acid, topiramate and 18-crown-6, 5-fluorouracil and urea, hydrochlorothiazide and nicotinic acid, hydrochlorothiazide and 18-crown-6, hydrochlorothiazide and piperazine, acetaminophen and 4,4'-bipyridine, phenytoin and pyridone, aspirin and 4,4'-bipyridine, ibuprofen and 4,4'-bipyridine, flurbiprofen and 4,4'-bipyridine, flurbiprofen and trans-1,2-bis(4-pyridyl) ethylene, carbamazepine and p-phthalaldehyde, carbamazepine and 2,6-pyridinecarboxylic acid, carbamazepine and 5-nitroisophthalic acid, carbamazepine and 1,3,5,7-adamantane tetracarboxylic acid, or carbamazepine and benzoquinone.

23. A process for modulating the solubility of an API for use in a pharmaceutical composition, which process comprises:

- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
- (b) isolating the co-crystal, wherein the co-crystal has a modulated solubility as compared to the API; and
- (c) incorporating the co-crystal having modulated solubility into a pharmaceutical composition.

24. The process of claim 23, wherein the solubility of the co-crystal is increased as compared to the API.

25. A process for modulating the dose response of an API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has a modulated dose response as compared to the API; and
  - (c) incorporating the co-crystal having modulated dose response into a pharmaceutical composition.
26. The process of claim 25, wherein the dose response of the co-crystal is increased as compared to the API.
27. A process for modulating the dissolution of an API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has a modulated dissolution as compared to the API; and
  - (c) incorporating the co-crystal having modulated dissolution into a pharmaceutical composition.
28. The process of claim 27, wherein the dissolution of the co-crystal is increased as compared to the API.
29. A process for modulating the bioavailability of an API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has a modulated bioavailability as compared to the API; and

- (c) incorporating the co-crystal having modulated bioavailability into a pharmaceutical composition.
30. The process of claim 29, wherein the bioavailability of the co-crystal is increased as compared to the API.
31. A process for increasing the stability of an API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has increased stability as compared to the API; and
  - (c) incorporating the co-crystal having increased stability into a pharmaceutical composition.
32. A process for the incorporation of a difficult to salt or unsaltable API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal;
  - (c) incorporating the co-crystal having a difficult to salt or unsaltable API into a pharmaceutical composition.
33. A process for decreasing the hygroscopicity of an API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has decreased hygroscopicity as compared to the API; and
  - (c) incorporating the co-crystal having decreased hygroscopicity into a pharmaceutical composition.

34. A process for crystallizing an amorphous API for use in a pharmaceutical composition, which process comprises:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal;
  - (c) incorporating the co-crystal into a pharmaceutical composition.
35. A process for decreasing the form diversity of an API for use in a pharmaceutical composition, which process includes:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has decreased form diversity as compared to the API; and
  - (c) incorporating the co-crystal having decreased form diversity into a pharmaceutical composition.
36. A process for modulating the morphology of an API for use in a pharmaceutical composition, which process includes:
- (a) contacting in solution the API with a co-crystal forming compound under crystallization conditions, so as to form a co-crystal of the API and the co-crystal forming compound;
  - (b) isolating the co-crystal, wherein the co-crystal has a different morphology as compared to the API; and
  - (c) incorporating the co-crystal having modulated morphology into a pharmaceutical composition.
37. The co-crystal of claim 1, specifically excluding a co-crystal selected from the group consisting of: nabumetone:2,3-naphthalenediol, fluoxetine HCl:benzoic acid, fluoxetine HCl:succinic acid, acetaminophen:piperazine, acetaminophen:theophylline, theophylline:salicylic acid, theophylline:p-hydroxybenzoic acid, theophylline:sorbic acid, theophylline:1-hydroxy-2-naphthoic acid, theophylline:glycolic acid,



theophylline:2,5-dihydroxybenzoic acid, theophylline:chloroacetic acid,  
 bis(diphenylhydantoin):9-ethyladenine acetylacetone solvate, bis(diphenylhydantoin):9-ethyladenine 2,4-pentanedione solvate, 5,5-diphenylbarbituric acid:9-ethyladenine,  
 bis(diphenylhydantoin):9-ethyladenine, 4-aminobenzoic acid:4-aminobenzonitrile,  
 sulfadimidine:salicylic acid, 8-hydroxyquinolinium 4-nitrobenzoate:4-nitrobenzoic acid,  
 sulfaproxyline:caffeine, retro-inverso-isopropyl (2R,3S)-4-cyclohexyl-2-hydroxy-3-(N-((2R)-2-morpholinocarbonylmethyl-3-(1-naphthyl)propionyl)-L-histidylamino)butyrate:cinnamic acid monohydrate, benzoic acid:isonicotinamide, 3-(2-N',N'-(dimethylhydrazino)-4-thiazolylmethylthio)-N''-sulfamoylpropionamide:maleic acid, diglycine hydrochloride ( $C_2H_5NO_2:C_2H_6NO_2^+Cl^-$ ),  
 octadecanoic acid:3-pyridinecarboxamide, cis-N-(3-methyl-1-(2-(1,2,3,4-tetrahydro)naphthyl)-piperidin-4-yl)-N-phenylpropanamide hydrochloride:oxalic acid,  
 trans-N-(3-methyl-1-(2-(1,2,3,4-tetrahydro)naphthyl)-piperidin-4-yl)-N-phenylpropanamide oxalate:oxalic acid dihydrate, bis(1-(3-((4-(2-isopropoxyphenyl)-1-piperazinyl)methyl)benzoyl)piperidine) succinate:succinic acid, bis(p-cyanophenyl)imidazolylmethane:succinic acid, cis-1-((4-(1-imidazolylmethyl)cyclohexyl)methyl)imidazole:succinic acid, (+)-2-(5,6-dimethoxy-1,2,3,4-tetrahydro-1-naphthyl)imidazoline:(+)-dibenzoyl-D-tartaric acid,  
 raclopride:tartaric acid, 2,6-diamino-9-ethylpurine:5,5-diethylbarbituric acid, 5,5-diethylbarbituric acid:bis(2-aminopyridine), 5,5-diethylbarbituric acid:acetamide, 5,5-diethylbarbituric acid:KI<sub>3</sub>, 5,5-diethylbarbituric acid:urea,  
 bis(barbital):hexamethylphosphoramide, 5,5-diethylbarbituric acid:imidazole, barbital:1-methylimidazole, 5,5-diethylbarbituric acid:N-methyl-2-pyridone, 2,4-diamino-5-(3,4,5-trimethoxybenzyl)-pyrimidine:5,5-diethylbarbituric acid,  
 bis(barbital):caffeine, bis(barbital):1-methylimidazole, bis(beta-cyclodextrin):bis(barbital) hydrate, tetrakis(beta-cyclodextrin):tetrakis(barbital), 9-ethyladenine:5,5-diethylbarbituric acid, barbital:N'-(p-cyanophenyl)-N-(p-iodophenyl)melamine, barbital:2-amino-4-(m-bromophenylamino)-6-chloro-1,3,5-triazine, 5,5-diethylbarbituric acid:N,N'-diphenylmelamine, 5,5-diethylbarbituric acid:N,N'-bis(p-chlorophenyl)melamine, N,N'-bis(p-bromophenyl)melamine:5,5-diethylbarbituric acid, 5,5-diethylbarbituric acid:N,N'-bis(p-iodophenyl)melamine, 5,5-diethylbarbituric acid:N,N'-bis(p-tolyl)melamine, 5,5-diethylbarbituric acid:N,N'-bis(m-tolyl)melamine, 5,5-diethylbarbituric acid:N,N'-bis(m-chlorophenyl)melamine, N,N'-Bis(m-methylphenyl)melamine:barbital, N,N'-bis(m-

chlorophenyl)melamine:barbital tetrahydrofuran solvate, 5,5-diethylbarbituric acid:N,N'-bis(t-butyl)melamine, 5,5-diethylbarbituric acid:N,N'-di(t-butyl)melamine, 6,6'-diquinolyl ether:5,5-diethylbarbituric acid, 5-t-butyl-2,4,6-triaminopyrimidine:diethylbarbituric acid, N,N'-bis(4-carboxymethylphenyl)melamine:barbital ethanol solvate, N,N'-bis(4-t-butylphenyl)melamine:barbital, tris(5,17-N,N'-bis(4-amino-6-(butylamino)-1,3,5-triazin-2-yl)diamino-11,23-dinitro-25,26,27,28-tetrapropoxycalix(4)arene):hexakis(diethylbarbituric acid) toluene solvate, N,N'-bis(m-fluorophenyl)melamine:barbital, N,N'-bis(m-bromophenyl)melamine:barbital acetone solvate, N,N'-bis(m-iodophenyl)melamine:barbital acetonitrile solvate, N,N'-bis(m-trifluoromethylphenyl)melamine:barbital acetonitrile solvate, aminopyrine:barbital, N,N'-bis(4-fluorophenyl)melamine:barbital, N,N'-bis(4-trifluoromethylphenyl)melamine:barbital, 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine:barbital, hydroxybutyrate:hydroxyvalerate, 2-aminopyrimidine:succinic acid, 1,3-bis(((6-methylpyrid-2-yl)amino)carbonyl)benzene:glutaric acid, 5-t-butyl-2,4,6-triaminopyrimidine:diethylbarbituric acid, bis(dithiobiuret-S,S')nickel(II):diuracil, platinum 3,3'-dihydroxymethyl-2,2'-bipyridine dichloride:AgF<sub>3</sub>CSO<sub>3</sub>, 4,4'-bipyridyl:isophthalic acid, 4,4'-bipyridyl:1,4-naphthalenedicarboxylic acid, 4,4'-bipyridyl:1,3,5-cyclohexane-tricarboxylic acid, 4,4'-bipyridyl:tricarballic acid, urotropin:azelaic acid, insulin:C8-HI (octanoyl-N<sup>c</sup>-LysB29-human insulin), isonicotinamide:cinnamic acid, isonicotinamide:3-hydroxybenzoic acid, isonicotinamide:3-N,N-dimethylaminobenzoic acid, isonicotinamide:3,5-bis(trifluoromethyl)-benzoic acid, isonicotinamide:d,l-mandelic acid, isonicotinamide:chloroacetic acid, isonicotinamide:fumaric acid monoethyl ester, isonicotinamide:12-bromododecanoic acid, isonicotinamide:fumaric acid, isonicotinamide:succinic acid, isonicotinamide:4-ketopimelic acid, isonicotinamide:thiodiglycolic acid, 1,3,5-cyclohexane-tricarboxylic acid:hexamethyltetramine, 1,3,5-cyclohexane-tricarboxylic acid:4,7-phenanthroline, 4,7-phenanthroline:oxalic acid, 4,7-phenanthroline:terephthalic acid, 4,7-phenanthroline:1,3,5-cyclohexane-tricarboxylic acid, 4,7-phenanthroline:1,4-naphthalenedicarboxylic acid, pyrazine:methanoic acid, pyrazine:ethanoic acid, pyrazine:propanoic acid, pyrazine:butanoic acid, pyrazine:pentanoic acid, pyrazine:hexanoic acid, pyrazine:heptanoic acid, pyrazine:octanoic acid, pyrazine:nonanoic acid,

pyrazine:decanoic acid, diammine-(deoxy-quanyl-quanyl-N<sup>7</sup>,N<sup>7</sup>)-platinum:tris(glycine) hydrate, 2-aminopyrimidine:p-phenylenediacetic acid, bis(2-aminopyrimidin-1-ium)fumarate:fumaric acid, 2-aminopyrimidine:indole-3-acetic acid, 2-aminopyrimidine:N-methylpyrrole-2-carboxylic acid, 2-aminopyrimidine:thiophen-2-carboxylic acid, 2-aminopyrimidine:(+)-camphoric acid, 2,4,6-Trinitrobenzoic acid: 2-aminopyrimidine, 2-aminopyrimidine:4-aminobenzoic acid, 2-aminopyrimidine:bis(phenoxyacetic acid), 2-aminopyrimidine:(2,4-dichlorophenoxy)acetic acid, 2-aminopyrimidine:(3,4-dichlorophenoxy)acetic acid, 2-aminopyrimidine:indole-2-carboxylic acid, 2-aminopyrimidine:terephthalic acid, 2-aminopyrimidine:bis(2-nitrobenzoic acid), 2-aminopyrimidine:bis(2-aminobenzoic acid), 2-aminopyrimidine:3-aminobenzoic acid, 2-hexeneoic acid:isonicotinamide, 4-nitrobenzoic acid:isonicotinamide, 3,5-dinitrobenzoic acid:isonicotinamide:4-methylbenzoic acid, 2-amino-5-nitropyrimidine:2-amino-3-nitropyridine, 3,5-dinitrobenzoic acid:4-chlorobenzamide, 3-dimethylaminobenzoic acid:4-chlorobenzamide, fumaric acid:4-chlorobenzamide, oxine:4-nitrobenzoic acid, oxine:3,5-dinitrobenzoic acid, oxine:3,5-dinitrosalicylic acid, 3-[2-(N',N'-dimethylhydrazino)-4-thiazolylmethylthio]-N<sup>2</sup>-sulfamoylpropionamidine:maleic acid, 5-fluorouracil:9-ethylhypoxanthine, 5-fluorouracil:cytosine dihydrate, 5-fluorouracil:theophylline monohydrate, stearic acid:nicotinamide, cis-1-{[4-(1-imidazolylmethyl)cyclohexyl]methyl}imidazole:succinic acid, CGS18320B:succinic acid, sulfaproxyline:caffeine, 4-aminobenzoic acid:4-aminobenzonitrile, 3,5-dinitrobenzoic acid:isonicotinamide:3-methylbenzoic acid, 3,5-dinitrobenzoic acid:isonicotinamide:4-(dimethylamino)benzoic acid, 3,5-dinitrobenzoic acid:isonicotinamide:4-hydroxy-3-methoxycinnamic acid, isonicotinamide:oxalic acid, isonicotinamide:malonic acid, isonicotinamide:succinic acid, isonicotinamide:glutaric acid, isonicotinamide:adipic acid, benzoic acid:isonicotinamide, mazapertine:succinate, betaine:dichloronitrophenol, betainepyridine:dichloronitrophenol, betainepyridine:pentachlorophenol, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:methyl 2,4-dihydroxybenzoate, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:2,4-dihydroxypropiophenone, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:2,4-dihydroxyacetophenone, squaric acid:4,4'-dipyridylacetylene, squaric acid:1,2-bis(4-pyridyl)ethylene, chloranilic acid:1,4-bis[(4-pyridyl)ethynyl]benzene, 4,4'-bipyridine:phthalic acid, 4,4'-dipyridylacetylene:phthalic

acid, bis(pentamethylcyclopentadienyl)iron:bromanilic acid,  
bis(pentamethylcyclopentadienyl)iron:chloranilic acid,  
bis(pentamethylcyclopentadienyl)iron:cyananilic acid,  
pyrazinotetrathiafulvalene:chloranilic acid, phenol:pentafluorophenol, co-crystals of  
itraconazole, and co-crystals of topiramate.